November 3, 2004 Attorney Docket No. P25,984-A REI

In the Claims

Please amend Claims 1, 9, 30, 31 to 33, 46, 54, 66, 74, 86 to 89, 92, 93, and 96, as follows.

1. (Five times amended) A compound of the formula:

$$\begin{bmatrix} & & & & & \\ & & & & \\ & & & & \\ & & & & \\ & & & & \\ & & & & \\ & & & & \\ & & & & \\ & & & & \\ & & & & \\ & & & & \\ & & & & \\ & & & & \\ & & & & \\ & & \\ & & & \\ & & & \\ & & & \\ & & & \\ & & & \\ & & & \\ & & & \\ & & &$$

$$(Y)_{p} = (CH_{2})_{n}O$$

wherein,

X is -O-, -S-, -NH-,
$$[-N(R_2)]$$
 or $-N-R_2$;

 R_2 is selected from the group consisting of lower alkyl, aryl lower alkyl, aryl, (C_3-C_{10}) cycloalkyl, aroyl, (C_2-C_{11}) alkanoyl, and phenylsulfonyl groups;

aryl is as defined hereinafter;

p is 1 or 2;

November 3, 2004 Attorney Docket No. P25,984-A REI

Y is hydrogen, lower alkyl, hydroxy, chlorine, fluorine, bromine, iodine, lower alkoxy, trifluoromethyl, nitro, or amino, when p is 1;

Y is lower alkoxy when p is 2 and X is -O-;

$$[R_1 \text{ is } R_{20}, R_{21} \text{ or } R_{22}, \text{ wherein:}$$

$$R_{20}$$
 is -(CH₂)_n- where] n is 2, 3, 4, or 5;

 $[R_{21}]$ is

$$-CH_2-CH=CH-CH_2-$$

$$-CH_2-C \equiv C-CH_2-$$

$$-CH_2-CH=CH-CH_2-CH_2$$
,

$$-CH_2-CH_2-CH=CH-CH_2-$$

$$-CH_2-C \equiv C-CH_2-CH_2-$$
, or

$$-CH_2-CH_2-C \equiv C-CH_2$$
,

the -CH=CH- bond being cis or trans;

 R_{22} is R_{20} or R_{21} in which one or more carbon atoms of R_{20} or R_{21} are substituted by at least one C_1 - C_6 linear alkyl group, phenyl group, or

lower alkyleneyl
$$(Z_1)_p$$

where Z₁ is lower alkyl, -OH, lower alkoxy, -CF₃, -NO₂, -NH₂ or halogen, p is as previously defined;]

R is hydrogen, lower alkyl, lower alkoxy, hydroxyl, carboxyl, chlorine, fluorine, bromine, iodine, amino, lower mono or dialkylamino, nitro, lower alkyl thio, trifluoromethoxy, cyano, acylamino, trifluoromethyl, trifluoroacetyl, aminocarbonyl, [monoalkylaminocarbonyl, dialkylaminocarbonyl, formyl,]

November 3, 2004 Attorney Docket No. P25,984-A REI

$$-C(=O)$$
-alkyl, $-C(=O)$ -O-alkyl, $-C(=O)$ -aryl, $-C(=O)$ -heteroaryl, or $-CH(OR_7)$ -alkyl[,]; [$-C(=W)$ -alkyl, $-C(=W)$ -aryl, or

-C(=W)-heteroaryl;

wherein alkyl is lower alkyl; aryl is phenyl or

 R_5

wherein R₅ is hydrogen, lower alkyl, lower alkoxy, hydroxy, chlorine, fluorine, bromine, iodine, lower monoalkylamino, [lower dialkylamino,] nitro, cyano, trifluoromethyl, or trifluoromethoxy;

heteroaryl is

$$Q_3$$
 ;

$$Q_3$$
 is -O-, -S-, -NH-, or -CH=N-;

[W is CH₂ or CHR₈ or N-R₉;]

 R_7 is hydrogen, lower alkyl, or [alkanoyl] <u>lower alkyl-(C=O)-</u>;

[R₈ is lower alkyl;

 R_9 is hydroxy, alkoxy, or $-NHR_{10}$; and

 R_{10} is hydrogen, lower alkyl, C_1 - C_3 acyl, aryl,

-C(=O)-aryl or -C(=O)-heteroaryl,

where aryl and heteroaryl are as defined above;]

November 3, 2004 Attorney Docket No. P25,984-A REI

and

m is 1, 2, or 3;

with the exclusion of compounds wherein X is O or S, Y is hydrogen, and R is hydrogen, [C₁ = 14 C₄] C₁-C₄ alkyl, chlorine, fluorine, bromine, iodine, cyano, C₁ - C₄ alkoxy, or -COOR₂₃ where R₂₃ is H or C₁ - C₄ alkyl; with the exclusion of compounds wherein X is -S-, [R₁ is R₂₀,] R is H, and m=1; [all geometric, optical, and stereoisomers thereof,] or a pharmaceutically acceptable acid addition salt thereof.

Synnestvedt & Lechner Llp

Group Art Unit 1624 Reissue Application No. 09/708,475 November 3, 2004 Attorney Docket No. P25,984-A REI

9. (Amended Three Times) A compound as claimed in claim 1, wherein X is -O-, -S-, or -NH-; Y is H, Cl, F, or -CF₃; R is selected from the group consisting of hydrogen, C₁-C₃ alkyl, C₁-C₃ alkoxy, -OH, Cl, F, Br, I, [acyl,] C₁-C₃ monoalkylamino, acylamino, [-NO₂-,] -NO₂, -OCF₃, and -CF₃; and n is 2, 3, or 4.

November 3, 2004 Attorney Docket No. P25,984-A REI

30. (Amended Five Times) A pharmaceutical composition, which comprises a compound of the formula:

$$\begin{bmatrix} & & & & & \\ & & & & \\ & & & & \\ & & & & \\ & & & & \\ & & & & \\ & & & & \\ & & & & \\ & & & & \\ & & & & \\ & & & & \\ & & & & \\ & & & & \\ & & & & \\ & & & & \\ &$$

$$(Y)_{p} = \begin{pmatrix} (R)_{m} \\ N - (CH_{2})_{n}O \end{pmatrix}$$

wherein X is -O, -S-, -NH-, or $-N(R_2)$;

 R_2 is selected from the group consisting of lower alkyl, aryl lower alkyl, aryl, (C_3-C_{10}) cycloalkyl, aroyl, (C_2-C_{11}) alkanoyl, and phenylsulfonyl groups;

wherein aryl is as defined hereinafter;

p is 1 or 2;

Y is hydrogen, lower alkyl, hydroxy, chlorine, fluorine, bromine, iodine, lower alkoxy, trifluoromethyl, nitro, or amino, when p is 1;

Y is lower alkoxy when p is 2 and X is -O-;

November 3, 2004 Attorney Docket No. P25,984-A REI

[R₁ is R₂₀, R₂₁ or R₂₂, wherein:
R₂₀ is
$$-(CH_2)_n$$
 where] n is 2, 3, 4, or 5;
[R₂₁ is
 $-CH_2$ -C=CH-CH₂-,
 $-CH_2$ -C=C-CH₂-,
 $-CH_2$ -CH=CH-CH₂-,

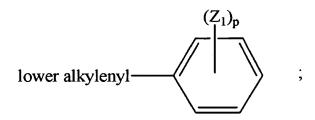
 $-CH_2-CH_2-CH=CH-CH_2-$

 $-CH_2-C \equiv C-CH_2-CH_2-$, or

 $-CH_2-CH_2-C \equiv C-CH_2$,

the -CH=CH- bond being cis or trans;

 R_{22} iS R_{20} or R_{21} in which one or more carbon atoms of R_{20} or R_{21} are substituted by at least on C_1 - C_6 linear alkyl group, phenyl group, or

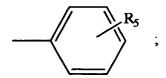


where Z₁ is lower alkyl, -OH, lower alkoxy, -CF₃, -NO₂, -NH₂ or halogen, and p as previously defined;]

R is hydrogen, lower alkyl, lower alkoxy, hydroxyl, carboxyl, chlorine, fluorine, bromine, iodine, amino, lower mono or dialkylamino, nitro, lower alkyl thio, trifluoromethoxy, cyano, acylamino, trifluoromethyl, trifluoroacetyl, aminocarbonyl, [monoalkylaminocarbonyl, dialkylaminocarbonyl, formyl,] -C(=O)-alkyl, -C(=O)-O-alkyl, -C(=O)-aryl, -C(=O)-heteroaryl, or $-CH(OR_7)-alkyl[,]; [-C(=W)-alkyl, -C(=W)-aryl, or$ -C(=W)-heteroaryl;]

November 3, 2004 Attorney Docket No. P25,984-A REI

alkyl is lower alkyl; aryl is phenyl or



where R₅ is hydrogen, lower alkyl, lower alkoxy, hydroxy, chlorine, fluorine, bromine, iodine, lower monoalkylamino, [lower dialkylamino,] nitro, cyano, trifluoromethyl, or trifluoromethoxy;

heteroaryl is

$$Q_3$$
 is -O-, -S-, -NH-, or -CH=N-;

[W is CH₂ or CHR₈ or N-R₉;]

 R_7 is hydrogen, lower alkyl, or $[(C_2-C_{11})$ alkanoyl] <u>lower</u> alkyl-(C=O)-;

[R₈ is lower alkyl;

R₉ is hydroxy, alkoxy, or -NHR₁₀; and

R₁₀ is hydrogen, lower alkyl, C₁-C₃ acyl, aryl,

-C(=O)-aryl or -C(=O)-heteroaryl,

where aryl and heteroaryl are as defined above;] and

m is 1, 2, or 3;

with the exclusion of compounds wherein X is O or S, Y is hydrogen, and R is

Synnestvedt & Lechner Llp

Group Art Unit 1624 Reissue Application No. 09/708,475 November 3, 2004 Attorney Docket No. P25,984-A REI

hydrogen, C_1 – C_4 alkyl, chlorine, fluorine, bromine, iodine, cyano, C_1 – C_4 alkoxy, or –COOR₂₃ where R_{23} is <u>H or C_1 – C_4 alkyl;</u>

with the exclusion of compounds wherein X is -S-, [R₁ is R₂₀,] R is H, and m=1; [all geometric, optical, and stereoisomers thereof,] or a pharmaceutically acceptable acid addition salt thereof, and a pharmaceutically acceptable carrier therefor.

31. (Amended Five Times) An antipsychotic composition, which comprises a compound of the formula:

$$(Y)_{p} = (R)_{m}$$

$$(R)_{m}$$

$$(R)_{m}$$

$$(Y)_{p} = \begin{pmatrix} (R)_{m} \\ N - (CH_{2})_{n}O - \end{pmatrix} \end{pmatrix} \end{pmatrix} \right)$$

wherein

X is -O-, -S-, -NH-, or -N(
$$R_2$$
);

 R_2 is selected from the group consisting of lower alkyl, aryl lower alkyl, aryl, (C_3-C_{10}) cycloalkyl, aroyl, (C_2-C_{11}) alkanoyl, and phenylsulfonyl groups; where <u>in</u> aryl is <u>as</u> defined hereinafter;

p is 1 or 2;

Y is hydrogen, lower alkyl, hydroxy, chlorine, fluorine, bromine, iodine, lower alkoxy, trifluoromethyl, nitro, or amino, when p is 1;

November 3, 2004 Attorney Docket No. P25,984-A REI

Y is lower alkoxy when p is 2 and X is -O-;

$$[R_1 \text{ is } R_{20}, R_{21} \text{ or } R_{22}, \text{ wherein:}$$

$$R_{20}$$
 is -(CH₂)_n- where] n is 2, 3, 4, or 5;

 $[R_{21}]$ is

$$-CH_2-CH=CH-CH_2-$$

$$-CH_2-C \equiv C-CH_2-$$

$$-CH_2-CH=CH-CH_2-CH_2$$

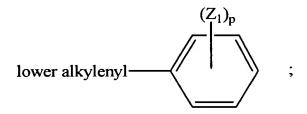
$$-CH_2-CH_2-CH=CH-CH_2-$$

$$-CH_2-C \equiv C-CH_2-CH_2-$$
, or

$$-CH_2-CH_2-C \equiv C-CH_2$$
,

the -CH=CH- bond being cis or trans;

 R_{22} is R_{20} or R_{21} in which one or more carbon atoms of R_{20} or R_{21} are substituted by at least on C_1 - C_6 linear alkyl group, phenyl group, or



where Z₁ is lower alkyl, -OH, lower alkoxy, -CF₃, -NO₂, -NH₂ or halogen, a p is as previously defined;]

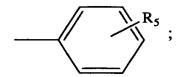
R is hydrogen, lower alkyl, lower alkoxy, hydroxyl, carboxyl, chlorine, fluorine, bromine, iodine, amino, lower mono or dialkylamino, nitro, lower alkyl thio, trifluoromethoxy, cyano, acylamino, trifluoromethyl, trifluoroacetyl, aminocarbonyl, [monoalkylaminocarbonyl, dialkylaminocarbonyl, formyl,] -C(=O)-alkyl, -C(=O)-O-alkyl, -C(=O)-aryl, -C(=O)-heteroaryl, or $-CH(OR_7)-alkyl[,]; [-C(=W)-alkyl, -C(=W)-aryl, or$

November 3, 2004 Attorney Docket No. P25,984-A REI

-C(=W)-heteroaryl;]

alkyl is lower alkyl;

aryl is phenyl or



where R₅ is hydrogen, lower alkyl, lower alkoxy, hydroxy, chlorine, fluorine, bromine, iodine, lower monoalkylamino, [lower dialkylamino,] nitro, cyano, trifluoromethyl, or trifluoromethoxy;

heteroaryl is

 Q_3 is -O-, -S-, -NH-, or -CH=N-;

[W is CH₂ or CHR₈ or N-R₉;]

 R_7 is hydrogen, lower alkyl, or $[(C_2-C_{11})$ alkanoyl] <u>lower</u> alkyl-(C=O)-;

[R₈ is lower alkyl;

 R_9 is hydroxy, alkoxy, or -NHR $_{10}$; and

 R_{10} is hydrogen, lower alkyl, C_1 - C_3 acyl, aryl,

-C(=O)-aryl or -C(=O)-heteroaryl,

where aryl and heteroaryl are as defined above;]

and

m is 1, 2, or 3;

November 3, 2004 Attorney Docket No. P25,984-A REI

with the exclusion of compounds wherein X is O or S, Y is hydrogen, and R is hydrogen, C₁-C₄ alkyl, chlorine, fluorine, bromine, iodine, cyano, C₁ - C₄ alkoxy, or -COOR₂₃ where R₂₃ is <u>H or C₁ - C₄ alkyl</u>;

with the exclusion of compounds wherein X is -S-, [R₁ is R₂₀,] R is H, and m=1; [all geometric, optical, and stereoisomers thereof,] or a pharmaceutically acceptable acid addition salt thereof, in an amount sufficient to produce an antipsychotic effect, and a pharmaceutically acceptable carrier therefor.

November 3, 2004 Attorney Docket No. P25,984-A REI

32. (Amended Four Times) A method of treating psychoses, which comprises administering to a mammal a psychoses-treating effective amount of a compound of the formula:

$$(Y)_{p} = (R)_{m}$$

$$(X)_{p} = (R)_{m}$$

$$(Y)_{p} \underbrace{\hspace{1cm} (CH_{2})_{n}O}_{N} \underbrace{\hspace{1cm} (CH_{2})_{n}O}_{N} \underbrace{\hspace{1cm} (R)_{m}}_{N}$$

wherein

X is -O-, -S-, -NH-, or -N(
$$R_2$$
);

 R_2 is selected from the group consisting of lower alkyl, aryl lower alkyl, aryl, (C_3-C_{10}) cycloalkyl, aroyl, (C_2-C_{11}) alkanoyl, and phenylsulfonyl groups;

where aryl is as defined hereinafter;

p is 1 or 2;

Y is hydrogen, lower alkyl, hydroxy, chlorine, fluorine, bromine, iodine, lower

November 3, 2004 Attorney Docket No. P25,984-A REI

alkoxy, trifluoromethyl, nitro, or amino, when p is 1;

Y is lower alkoxy when p is 2 and X is -O-:

$$[R_1 \text{ is } R_{20}, R_{21} \text{ or } R_{22}, \text{ wherein:}$$

$$R_{20}$$
 is -(CH₂)_n- where] n is 2, 3, 4, or 5;

 $[R_{21}]$ is

$$-CH_2-CH=CH-CH_2-$$

$$-CH_2-C\equiv C-CH_2-$$

$$-CH_2-CH=CH-CH_2-CH_2$$
,

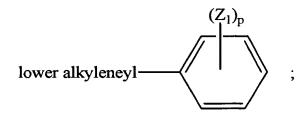
$$-CH_2-CH_2-CH=CH-CH_2-$$

$$-CH_2-C \equiv C-CH_2-CH_2-$$
, or

$$-CH_2-CH_2-C \equiv C-CH_2$$
,

the -CH=CH- bond being cis or trans;

 R_{22} is R_{20} or R_{21} in which one or more carbon atoms of R_{20} or R_{22} are substituted by at least on C_1 - C_6 linear alkyl group, phenyl group, or



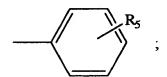
where Z₁ is lower alkyl, -OH, lower alkoxy, -CF₃, -NO₂, -NH₂ or halogen, and p is as previously defined;]

R is hydrogen, lower alkyl, lower alkoxy, hydroxyl, carboxyl, chlorine, fluorine, bromine, iodine, amino, lower mono or dialkylamino, nitro, lower alkyl thio, trifluoromethoxy, cyano, acylamino, trifluoromethyl, trifluoroacetyl, aminocarbonyl, [monoalkylaminocarbonyl, dialkylaminocarbonyl, formyl,] -C(=O)-alkyl, -C(=O)-O-alkyl, -C(=O)-aryl, -C(=O)-heteroaryl, or

November 3, 2004 Attorney Docket No. P25,984-A REI

$$-CH(OR_7)$$
-alkyl[,]; [-C(=W)-alkyl, -C(=W)-aryl, or -C(=W)-heteroaryl;]

wherein alkyl is lower alkyl; aryl is phenyl or



where<u>in</u> R₅ is hydrogen, lower alkyl, lower alkoxy, hydroxy, chlorine, fluorine, bromine, iodine, lower monoalkylamino, [lower dialkylamino,] nitro, cyano, trifluoromethyl, or trifluoromethoxy;

heteroaryl is

$$Q_3$$
 is -O-, -S-, -NH-, or -CH=N-;

[W is CH₂ or CHR₈ or N-R₉;]

 R_7 is hydrogen, lower alkyl, or $[(C_2-C_{11})$ alkanoyl] <u>lower alkyl-(C=O)-;</u>

[R₈ is lower alkyl;

 R_9 is hydroxy, alkoxy, or -NHR₁₀; and

 R_{10} is hydrogen, lower alkyl, C_1 - C_3 acyl, aryl,

-C(=O)-aryl or -C(=O)-heteroaryl,

where aryl and heteroaryl are as defined above;]

Synnestvedt & Lechner Llp

Group Art Unit 1624 Reissue Application No. 09/708,475 November 3, 2004 Attorney Docket No. P25,984-A REI

and

m is 1, 2, or 3;

with the exclusion of compounds wherein X is O or S, Y is hydrogen, and R is hydrogen, C₁-C₄ alkyl, chlorine, fluorine, bromine, iodine, cyano, C₁-C₄ alkoxy, or -COOR₂₃

wherein R₂₃ is H or C₁-C₄ alkyl;

with the exclusion of compounds wherein X is -S-, [R₁ is R₂₀,] R is H, and m=1; [all geometric, optical, and stereoisomers thereof,] or a pharmaceutically acceptable acid addition salt thereof.

November 3, 2004 Attorney Docket No. P25,984-A REI

33. (Amended Four Times) An analgesic composition, which comprises a compound of the formula:

$$(Y)_{p} = (R)_{m}$$

$$(X)_{p} = (R)_{m}$$

$$(Y)_{p} = (CH_{2})_{n}O$$

wherein,

X is -O-, -S-, -NH-, or
$$[-N(R_2)] \frac{|}{-N(R_2)}$$
;

 R_2 is selected from the group consisting of lower alkyl, aryl lower alkyl, aryl, (C_3-C_{10}) cycloalkyl, aroyl, (C_2-C_{11}) alkanoyl, and phenylsulfonyl groups;

wherein aryl is as defined hereinafter;

p is 1 or 2;

Y is hydrogen, lower alkyl, hydroxy, chlorine, fluorine, bromine, iodine, lower alkoxy, trifluoromethyl, nitro, or amino, when p is 1;

November 3, 2004 Attorney Docket No. P25,984-A REI

Y is lower alkoxy when p is 2 and X is -O-;

$$[R_1 \text{ is } R_{20}, R_{21} \text{ or } R_{22}, \text{ wherein:}$$

$$R_{20}$$
 is $-(CH_2)_n$ - where] n is 2, 3, 4, or 5; $[R_{21}$ is

$$-CH_2-CH=CH-CH_2-$$

$$-CH_2-C \equiv C-CH_2-$$

$$-CH_2-CH=CH-CH_2-CH_2$$

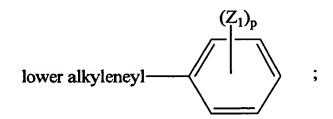
$$-CH_2-CH_2-CH=CH-CH_2-$$

$$-CH_2-C \equiv C-CH_2-CH_2-$$
, or

$$-CH_2-CH_2-C \equiv C-CH_2$$
,

the -CH=CH- bond being cis or trans;

 R_{22} is R_{20} or R_{21} in which one or more carbon atoms of R_{20} or R_{21} are substituted by at least on C_1 - C_6 linear alkyl group, phenyl group, or

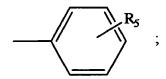


where Z_1 is lower alkyl, -OH, lower alkoxy, -CF₃, -NO₂, -NH₂ or halogen, and p is as previously defined;]

R is hydrogen, lower alkyl, lower alkoxy, hydroxyl, carboxyl, chlorine, fluorine, bromine, iodine, amino, lower mono or dialkylamino, nitro, lower alkyl thio, trifluoromethoxy, cyano, acylamino, trifluoromethyl, trifluoroacetyl, aminocarbonyl, [monoalkylaminocarbonyl, dialkylaminocarbonyl, formyl,] -C(=O)-alkyl, -C(=O)-O-alkyl, -C(=O)-aryl, -C(=O)-heteroaryl, or

November 3, 2004 Attorney Docket No. P25,984-A REI

-CH(OR₇)-alkyl[,]; [-C(=W)-alkyl, -C(=W)-aryl, or-C(=W)-heteroaryl;] wherein alkyl is lower alkyl; aryl is phenyl or



where<u>in</u> R₅ is hydrogen, lower alkyl, lower alkoxy, hydroxy, chlorine, fluorine, bromine, iodine, lower monoalkylamino, [lower dialkylamino,] nitro, cyano, trifluoromethyl, or trifluoromethoxy;

heteroaryl is

$$Q_3$$

wherein Q_3 is -O-, -S-, -NH-, or -CH=N-;

[W is CH₂ or CHR₈ or N-R₉;]

 R_7 is hydrogen, lower alkyl, or $[(C_2-C_{11})$ alkanoyl] <u>lower alkyl-(C=O)-;</u> $[R_8$ is lower alkyl;

R₉ is hydroxy, alkoxy, or -NHR₁₀; and

 R_{10} is hydrogen, lower alkyl, C_1 - C_3 acyl, aryl,

-C(=O)-aryl or -C(=O)-heteroaryl,

where aryl and heteroaryl are as defined above;] and

m is 1, 2, or 3;

Synnestvedt & Lechner Llp

Group Art Unit 1624 Reissue Application No. 09/708,475 November 3, 2004 Attorney Docket No. P25,984-A REI

with the exclusion of compounds wherein X is O or S, Y is hydrogen, and R is hydrogen, C₁-C₄ alkyl, chlorine, fluorine, bromine, iodine, cyano, C₁-C₄ alkoxy, or -COOR₂₃

wherein R₂₃ is H or C₁-C₄ alkyl;

with the exclusion of compounds wherein X is -S-, [R₁ is R₂₀,] R is H, and m=1; [all geometric, optical, and stereoisomers thereof,] or a pharmaceutically acceptable acid addition salt thereof, in an amount sufficient to produce a pain-relieving effect, and a pharmaceutically acceptable carrier therefor.

November 3, 2004 Attorney Docket No. P25,984-A REI

46. (Amended Twice) A compound of the formula

$$(Y)_{p} \underbrace{\qquad \qquad \qquad \qquad \qquad }_{X} N \underbrace{\qquad \qquad N - (R_{1}) - O - \underbrace{\qquad \qquad }_{Q} N}_{Q}$$

wherein

 $X \text{ is } -O_{-}, -S_{-}, -NH_{-}, \text{ or } -N(R_{2});$

 R_2 is selected from the group consisting of lower alkyl, aryl lower alkyl, aryl, (C_3-C_{10}) cycloalkyl, aroyl, (C_2-C_{11}) alkanoyl, and phenylsulfonyl groups;

aryl is as defined hereinafter;

p is 1 or 2;

Y is hydrogen, lower alkyl, hydroxy, chlorine, fluorine, bromine, iodine, lower alkoxy, trifluoromethyl, nitro, or amino, when p is 1;

Y is lower alkoxy, hydroxy, or halogen when p is 2 and X is -O-;

(R_1) is

 $-CH_2-CH=CH-CH_2-$

 $-CH_2-C \equiv C-CH_2-$

 $-CH_2-CH=CH-CH_2-CH_2-.$

 $-CH_2-CH_2-CH=CH-CH_2-$

 $-CH_2-C \equiv C-CH_2-CH_2-$, or

 $-CH_2-CH_2-C \equiv C-CH_2-$

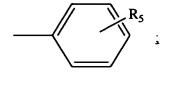
November 3, 2004 Attorney Docket No. P25,984-A REI

the -CH=CH- bond being cis or trans:

R is hydrogen, lower alkyl, lower alkoxy, hydroxyl, carboxyl, chlorine, fluorine, bromine, iodine, amino, lower mono or dialkylamino, nitro, lower alkyl thio, trifluoromethoxy, cyano, acylamino, trifluoromethyl, trifluoroacetyl, aminocarbonyl, dialkylaminocarbonyl, formyl, -C(=O)-alkyl, -C(=O)-alkyl, -C(=O)-aryl, -C(=O)-heteroaryl, -CH(OR₇)-alkyl, -C(=W)-alkyl, -C(=W)-aryl, or -C(=W)-heteroaryl;

wherein alkyl is lower alkyl;

aryl is phenyl or



wherein R₅ is hydrogen, lower alkyl, lower alkoxy, hydroxy,

chlorine, fluorine, bromine, iodine, lower

monoalkylamino, lower dialkylamino, nitro,

trifluoromethyl, or trifluoromethoxy;

cyano,

heteroaryl is

wherein Q_3 is -O-, -S-, -NH-, or -CH=N-;

W is CH₂ or CHR₈ or N-R₉;

 R_7 is hydrogen, lower alkyl, or lower alkyl-(C=O)-;

Synnestvedt & Lechner Llp

Group Art Unit 1624 Reissue Application No. 09/708,475

November 3, 2004 Attorney Docket No. P25,984-A REI

R₈ is lower alkyl;

R₉ is hydroxy, lower alkoxy, or -NHR₁₀; and

R₁₀ is hydrogen, lower alkyl, C_1 - C_3 acyl, aryl, -C(=O)-aryl, or -C(=O)-heteroaryl,

wherein aryl and heteroaryl are as defined above; and

m is 1, 2, or 3;

with the exclusion of compounds wherein X is O or S, Y is hydrogen, and R is

hydrogen, C₁-C₄ alkyl, chlorine, fluorine, bromine, iodine, cyano, C₁-C₄

alkoxy, or -COOR₂₃

wherein R_{23} is H or C_1 - C_4 alkyl;

all geometric, optical and stereoisomers thereof, or a pharmaceutically acceptable acid addition salt thereof.

Synnestvedt & Lechner Llp

Group Art Unit 1624 Reissue Application No. 09/708,475 November 3, 2004 Attorney Docket No. P25,984-A REI

54. (Amended Twice) A compound as claimed in claim 46, wherein X is -O-, -S-, or -NH-; Y is H, Cl, F, or -CF₃; R is selected from the group consisting of hydrogen, C₁-C₃ alkyl, C₁-C₃ alkoxy, -OH, Cl, F, Br, I, C₁-C₃ monoalkylamino, acylamino, -NO₂, -OCF₃, and -CF₃.

November 3, 2004 Attorney Docket No. P25,984-A REI

66. (Amended Twice) A compound of the formula

wherein

X is $-O_{-}$, $-S_{-}$, $-NH_{-}$, or $-N(R_2)$;

 R_2 is selected from the group consisting of lower alkyl, aryl lower alkyl, aryl, $(C_3 - C_{10})$ cycloalkyl, aroyl, $(C_2 - C_{11})$ alkanoyl, and phenylsulfonyl groups; aryl is as defined hereinafter;

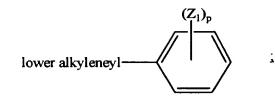
p is 1 or 2;

Y is hydrogen, lower alkyl, hydroxy, chlorine, fluorine, bromine, iodine, lower alkoxy, trifluoromethyl, nitro, or amino, when p is 1;

Y is lower alkoxy, hydroxy, or halogen when p is 2 and X is -O-;

 (R_1) is R_{20} or R_{21} in which one or more carbon atoms of R_{20} or R_{21} are substituted by at least one C_1 - C_6 linear alkyl group, phenyl group or

November 3, 2004 Attorney Docket No. P25,984-A REI



wherein Z₁ is lower alkyl, -OH, lower alkoxy, -CF₃, -NO₂, -NH₂ or halogen;

 R_{20} is $-(CH_2)_n$, where n is 2, 3, 4 or 5;

 R_{21} is

 $-CH_2-CH=CH-CH_2-$

 $-CH_2-C \equiv C-CH_2-$

 $-CH_2-CH=CH-CH_2-CH_2-$

 $-CH_2-CH_3-CH=CH-CH_3-$

 $-CH_2-C = C-CH_2-CH_2-$, or

 $-CH_2-CH_2-C \equiv C-CH_2-$

the -CH=CH- bond being cis or trans;

R is hydrogen, lower alkyl, lower alkoxy, hydroxyl, carboxyl, chlorine,

fluorine, bromine, iodine, amino, lower mono or dialkylamino, nitro, lower alkyl thio, trifluoromethoxy, cyano, acylamino, trifluoromethyl, trifluoroacetyl, aminocarbonyl, monoalkylaminocarbonyl,

dialkylaminocarbonyl, formyl, -C(=O) – alkyl, -C(=O) – O – alkyl,

-C(=O)-aryl, -C(=O)-heteroaryl, $-CH(OR_7)$ -alkyl, -C(=W)-alkyl,

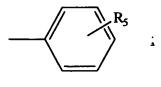
SYNNESTVEDT & LECHNER LLP

Group Art Unit 1624 Reissue Application No. 09/708,475 November 3, 2004 Attorney Docket No. P25,984-A REI

-C(=W)-aryl, or -C(=W)-heteroaryl;

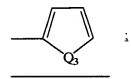
wherein alkyl is lower alkyl;

aryl is phenyl or



wherein R₅ is hydrogen, lower alkyl, lower alkoxy, hydroxy,
chlorine, fluorine, bromine, iodine, lower
monoalkylamino, lower dialkylamino, nitro, cyano,
trifluoromethyl, or trifluoromethoxy;

heteroaryl is



wherein Q_3 is -O-, -S-, -NH-, or -CH=N-;

W is CH₂ or CHR₈ or N-R₉;

 R_7 is hydrogen, lower alkyl, or lower alkyl-(C=O)-;

R₈ is lower alkyl;

R₉ is hydroxy, lower alkoxy, or -NHR₁₀; and

R₁₀ is hydrogen, lower alkyl, C_1 - C_3 acyl, aryl,

-C(=O)-aryl, or -C(=O)-heteroaryl,

November 3, 2004 Attorney Docket No. P25,984-A REI

wherein aryl and heteroaryl are as defined above; and

m is 1, 2, or 3;

with the exclusion of compounds wherein X is O or S, Y is hydrogen, and R is

hydrogen, C₁-C₄ alkyl, chlorine, fluorine, bromine, iodine, cyano, C₁-C₄

alkoxy, or -COOR₂₃

wherein R_{23} is H or C_1 - C_4 alkyl;

with the exclusion of compounds wherein X is -S-, R_1 is R_{20} , R is H, and m=1; all geometric, optical and stereoisomers thereof, or a pharmaceutically acceptable acid addition salt thereof.

Synnestvedt & Lechner Llp

Group Art Unit 1624 Reissue Application No. 09/708,475 November 3, 2004 Attorney Docket No. P25,984-A REI

74. (Amended Twice) A compound as claimed in claim 66, wherein X is -O-, -S-, or -NH-; Y is H, Cl, F, or -CF₃; R is selected from the group consisting of hydrogen, C₁-C₃ alkyl, C₁-C₃ alkoxy, -OH, Cl, F, Br, I, C₁-C₃ monoalkylamino, acylamino, -NO₂, -OCF₃, and -CF₃; and n is 2, 3, or 4.

November 3, 2004 Attorney Docket No. P25,984-A REI

86. (Amended) A pharmaceutical composition, which compromises a compound of the formula

$$(Y)_p$$
 $N-(R_1)-O$
 $N-(R_1)-O$

<u>wherein</u>

X is -O-, -S-, -NH-, or -N(R₂);

 R_2 is selected from the group consisting of lower alkyl, aryl lower alkyl, aryl, $(C_3 - C_{10})$ cycloalkyl, aroyl, $(C_2 - C_{11})$ alkanoyl, and phenylsulfonyl groups; aryl is defined hereinafter:

p is 1 or 2;

Y is hydrogen, lower alkyl, hydroxy, chlorine, fluorine, bromine, iodine, lower alkoxy, trifluoromethyl, nitro, or amino, when p is 1;

Y is lower alkoxy, hydroxy, or halogen when p is 2 and X is -O-;

 (R_1) is

-CH₂-CH=CH-CH₂-.

-CH2-C=C-CH2-

-CH,-CH=CH-CH,-CH,-

SYNNESTVEDT & LECHNER LLP

Group Art Unit 1624 Reissue Application No. 09/708,475

November 3, 2004 Attorney Docket No. P25,984-A REI

-CH₂-CH₂-CH=CH-CH₂-,

 $-CH_2-C \equiv C-CH_2-CH_2-$, or

-CH₂-CH₂-C≡C-CH₂-,

the -CH=CH- bond being cis or trans;

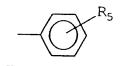
R is hydrogen, lower alkyl, lower alkoxy, hydroxyl, carboxyl, chlorine, fluorine, bromine, iodine, amino, lower mono or dialkylamino, nitro, lower alkyl thio, trifluoromethoxy, cyano, acylamino, trifluoromethyl, trifluoroacetyl, aminocarbonyl, dialkylaminocarbonyl, formyl,

-C(=O)-alkyl, -C(=O)-o-alkyl, -C(=O)-heteroaryl,

-CH(OR₇)-alkyl, -C(=W)-alkyl, -C(=W)-aryl, or -C(=W)-heteroaryl;

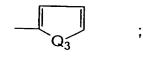
where alkyl is lower alkyl;

aryl is phenyl or



where R₅ is hydrogen, lower alkyl, lower alkoxy, hydroxy, chlorine, fluorine, bromine, iodine, lower monoalkylamino, lower dialkylamino, nitro, cyano, trifluoromethyl, trifluoromethoxy;

heteroaryl is



November 3, 2004 Attorney Docket No. P25,984-A REI

where Q₃ is -O-, -S-, -NH-, or -CH=N-;

W is CH₂ or CHR₈ or N-R₉;

R₇ is hydrogen, lower alkyl, or lower alkyl-(C=O)-;

R₈ is lower alkyl;

R₉ is hydroxy, lower alkoxy, or -NHR₁₀; and

R₁₀ is hydrogen, lower alkyl, C₁-C₃ acyl, aryl,

-C(=O)-aryl, or -C(=O)-heteroaryl,

where aryl and heteroaryl are as defined above; and

m is 1, 2, or 3;

with the exclusion of compounds wherein X is O or S, Y is hydrogen, and R is hydrogen, $C_1-C_4 \text{ alkyl, chlorine, fluorine, bromine, iodine, cyano, } C_1-C_4 \text{ alkoxy, or -COOR}_{23}$ where R_{23} is C_1-C_4 alkyl;

all geometric, optical and stereoisomers thereof, or a pharmaceutically acceptable acid addition salt thereof, and a pharmaceutically acceptable carrier therefor.

November 3, 2004 Attorney Docket No. P25,984-A REI

87. (Amended) A pharmaceutical composition, which comprises a compound of the formula

$$(Y)_p$$
 $N-(R_1)-O$
 $N-(R_1)$

wherein

X is -O-, -S-, -NH-, or -N(R_2);

R₂ is selected from the group consisting of lower alkyl, aryl lower alkyl, aryl, (C₃-

 C_{10})cycloalkyl, aroyl, (C_2-C_{11}) alkanoyl, and phenylsulfonyl groups;

aryl is defined hereinafter;

p is 1 or 2;

Y is hydrogen, lower alkyl, hydroxy, chlorine, fluorine, bromine, iodine, lower alkoxy, trifluoromethyl, nitro, or amino, when p is 1;

Y is lower alkoxy, hydroxy, or halogen when p is 2 and X is -O-;

(R₁) is R_{20} or R_{21} in which one or more carbon atoms of R_{20} or R_{21} are substituted by at least one C_1 - C_6 linear alkyl group, phenyl group or

November 3, 2004 Attorney Docket No. P25,984-A REI

where Z_1 is lower alkyl, -OH, lower alkoxy, -CF₃, -NO₂, -NH₂ or halogen; R_{20} is -(CH₂)_n-, where n is 2, 3, 4 or 5;

 R_{21} is

-CH₂-CH=CH-CH₂-,

-CH₂-C≅C-CH₂-,

-CH₂-CH=CH-CH₂-CH₂-,

-CH₂-CH₂-CH=CH-CH₂-,

 $-CH_2-C = C-CH_2-CH_2-$, or

-CH₂-CH₂-C≡C-CH₂-,

the -CH=CH- bond being cis or trans;

R is hydrogen, lower alkyl, lower alkoxy, hydroxyl, carboxyl, chlorine, fluorine, bromine,

iodine, amino, lower mono or dialkylamino, nitro, lower alkyl thio,

trifluoromethoxy, cyano, acylamino, trifluoromethyl, trifluoroacetyl,

aminocarbonyl, monoalkylaminocarbonyl, dialkylaminocarbonyl, formyl,

-C(=O)-alkyl, -C(=O)-O-alkyl, -C(=O)-aryl, -C(=O)-heteroaryl,

 $-CH(OR_7)$ -alkyl, -C(=W)-alkyl, -C(=W)-aryl, or -C(=W)-heteroaryl;

November 3, 2004 Attorney Docket No. P25,984-A REI

where alkyl is lower alkyl;

aryl is phenyl or

$$R_5$$

where R₅ is hydrogen, lower alkyl, lower alkoxy, hydroxy, chlorine, fluorine, bromine, iodine, lower monoalkylamino, lower dialkylamino, nitro, cyano, trifluoromethyl, trifluoromethoxy;

heteroaryl is

$$Q_3$$

where Q₃ is -O-, -S-, -NH-, or -CH=N-;

W is CH₂ or CHR₈ or N-R₉;

R₇ is hydrogen, lower alkyl-(C=O)-:

R₈ is lower alkyl;

R₉ is hydroxy, lower alkoxy, or -NHR₁₀; and

 R_{10} is hydrogen, lower alkyl, C_1 - C_3 acyl, aryl,

-C(=O)-aryl, or -C(=O)-heteroaryl,

where aryl and heteroaryl are as defined above; and

November 3, 2004 Attorney Docket No. P25,984-A REI

m is 1, 2, or 3;

with the exclusion of compounds wherein X is O or S, Y is hydrogen, and R is hydrogen, C_1 - C_4 alkyl, chlorine, fluorine, bromine, iodine, cyano, C_1 - C_4 alkoxy, or -COOR, where R_{23} is C_1 - C_4 alkyl;

with the exclusion of compounds wherein X is -S-, R₁ is R₂₀, R is H, and m=1;

all geometric, optical and stereoisomers thereof, or a pharmaceutically acceptable acid

addition salt thereof, and a pharmaceutically acceptable carrier therefor.

88. (Amended) An antipsychotic composition, which comprises a compound of the formula

$$(Y)_p$$
 $N-(R_1)-O$
 $N-(R_1)$

wherein

X is $-O_{-}$, $-S_{-}$, $-NH_{-}$, or $-N(R_{2})$;

R₂ is selected from the group consisting of lower alkyl, aryl lower alkyl, aryl, (C₃-

 C_{10})cycloalkyl, aroyl, (C_2-C_{11}) alkanoyl, and phenylsulfonyl groups;

aryl is defined hereinafter;

p is 1 or 2;

November 3, 2004 Attorney Docket No. P25,984-A REI

Y is hydrogen, lower alkyl, hydroxy, chlorine, fluorine, bromine, iodine, lower alkoxy, trifluoromethyl, nitro, or amino, when p is 1;

Y is lower alkoxy, hydroxy, or halogen when p is 2 and X is -O-;

 (R_1) is

-CH₂-CH=CH-CH₂-,

 $-CH_2-C = C-CH_2-,$

-CH₂-CH=CH-CH₂

-CH₂-CH₂-CH=CH-CH₂-,

 $-CH_2-C \equiv C-CH_2-CH_2-$, or

 $-CH_2-CH_2-C = C-CH_2-$

the -CH=CH- bond being cis or trans;

R is hydrogen, lower alkyl, lower alkoxy, hydroxyl, carboxyl, chlorine, fluorine, bromine, iodine, amino, lower mono or dialkylamino, nitro, lower alkyl thio, trifluoromethoxy, cyano, acylamino, trifluoromethyl, trifluoroacetyl,

aminocarbonyl, dialkylaminocarbonyl, formyl,

-C(=O)-alkyl, -C(=O)-aryl, -C(=O)-heteroaryl,

 $-CH(OR_7)$ -alkyl, -C(=W)-alkyl, -C(=W)-aryl, or -C(=W)-heteroaryl;

where alkyl is lower alkyl;

aryl is phenyl or

November 3, 2004 Attorney Docket No. P25,984-A REI

where R₅ is hydrogen, lower alkyl, lower alkoxy, hydroxy, chlorine, fluorine, bromine, iodine, lower monoalkylamino, lower dialkylamino, nitro, cyano, trifluoromethyl, trifluoromethoxy;

heteroaryl is

$$Q_3$$

where Q_3 is -O-, -S-, -NH-, or -CH=N-;

W is CH₂ or CHR₈ or N-R₉;

R₇ is hydrogen, lower alkyl, or lower alkyl-(C=O)-:

R₈ is lower alkyl;

R₉ is hydroxy, lower alkoxy, or -NHR₁₀; and

R₁₀ is hydrogen, lower alkyl, C₁-C₃ acyl, aryl,

-C(=O)-aryl, or -C(=O)-heteroaryl,

where aryl and heteroaryl are as defined above; and

m is 1, 2, or 3;

with the exclusion of compounds wherein X is O or S, Y is hydrogen, and R is hydrogen, $C_1-C_4 \text{ alkyl, chlorine, fluorine, bromine, iodine, cyano, } C_1-C_4 \text{ alkoxy, or -COOR}_{23}$ where R_{23} is C_1-C_4 alkyl;

November 3, 2004 Attorney Docket No. P25,984-A REI

all geometric, optical and stereoisomers thereof, or a pharmaceutically acceptable acid

addition salt thereof, in an amount sufficient to produce an antipsychotic effect,

and a pharmaceutically acceptable carrier therefor.

89. (Amended) An antipsychotic composition, which comprises a compound of the formula

wherein

X is -O-, -S-, -NH-, or - $N(R_2)$;

R₂ is selected from the group consisting of lower alkyl, aryl lower alkyl, aryl, $(C_3$ - C_{10})cycloalkyl, aroyl, $(C_2$ - C_{11})alkanoyl, and phenylsulfonyl groups; aryl is defined hereinafter;

p is 1 or 2;

Y is hydrogen, lower alkyl, hydroxy, chlorine, fluorine, bromine, iodine, lower alkoxy, trifluoromethyl, nitro, or amino, when p is 1;

Y is lower alkoxy, hydroxy, or halogen when p is 2 and X is -O-;

 (R_1) is R_{20} or R_{21} in which one or more carbon atoms of R_{20} or R_{21} are substituted by at

November 3, 2004 Attorney Docket No. P25,984-A REI

least one C₁-C₆ linear alkyl group, phenyl group or

where Z₁ is lower alkyl, -OH, lower alkoxy, -CF₃, -NO₂, -NH₂ or halogen;

 R_{20} is -(CH₂)_n-, where n is 2, 3, 4 or 5;

 R_{21} is

-CH₂-CH=CH-CH₂-,

 $\underline{-CH_2-C} \equiv C-CH_2-\underline{,}$

-CH2-CH=CH-CH2-CH2-,

-CH2-CH2-CH=CH-CH2-,

 $-CH_2-C = C-CH_2-CH_2-$, or

 $-CH_2-CH_2-C = C-CH_2-,$

the -CH=CH- bond being cis or trans;

R is hydrogen, lower alkyl, lower alkoxy, hydroxyl, carboxyl, chlorine, fluorine, bromine,

iodine, amino, lower mono or dialkylamino, nitro, lower alkyl thio,

trifluoromethoxy, cyano, acylamino, trifluoromethyl, trifluoroacetyl,

aminocarbonyl, monoalkylaminocarbonyl, dialkylaminocarbonyl, formyl,

-C(=O)-alkyl, -C(=O)-o-alkyl, -C(=O)-heteroaryl,

 $-CH(OR_7)$ -alkyl, -C(=W)-aryl, or -C(=W)-heteroaryl;

November 3, 2004 Attorney Docket No. P25,984-A REI

where alkyl is lower alkyl;

aryl is phenyl or

$$R_5$$

where R₅ is hydrogen, lower alkyl, lower alkoxy, hydroxy, chlorine, fluorine, bromine, iodine, lower monoalkylamino, lower dialkylamino, nitro, cyano, trifluoromethyl, trifluoromethoxy;

heteroaryl is

$$Q_3$$

where Q_3 is -O-, -S-, -NH-, or -CH=N-;

W is CH₂ or CHR₈ or N-R₉;

R₇ is hydrogen, lower alkyl, or lower alkyl-(C=O)-;

R₈ is lower alkyl;

R₉ is hydroxy, lower alkoxy, or -NHR₁₀; and

R₁₀ is hydrogen, lower alkyl, C₁-C₃ acyl, aryl,

-C(=O)-aryl, or -C(=O)-heteroaryl,

where aryl and heteroaryl are as defined above; and

m is 1, 2, or 3;

with the exclusion of compounds wherein X is O or S, Y is hydrogen, and R is hydrogen, C_1 - C_4 alkyl, chlorine, fluorine, bromine, iodine, cyano, C_1 - C_4 alkoxy, or -COOR₂₃ where R_{23} is C_1 - C_4 alkyl;

with the exclusion of compounds wherein X is -S-, R₁ is R₂₀, R is H, and m=1;

all geometric, optical and stereoisomers thereof, or a pharmaceutically acceptable acid

addition salt thereof, in an amount sufficient to produce an antipsychotic effect,

and a pharmaceutically acceptable carrier therefor.

92. (Amended) An analgesic composition, which comprises a compound of the formula

$$(Y)_p$$
 $N-(R_1)-O$
 $N-(R_1)$

November 3, 2004 Attorney Docket No. P25,984-A REI

wherein :

X is -O-, -S-, -NH-, or - $N(R_2)$;

R, is selected from the group consisting of lower alkyl, aryl lower alkyl, aryl, (C3-

 C_{10})cycloalkyl, aroyl, (C_2-C_{11}) alkanoyl, and phenylsulfonyl groups;

aryl is defined hereinafter;

p is 1 or 2;

Y is hydrogen, lower alkyl, hydroxy, chlorine, fluorine, bromine, iodine, lower alkoxy, trifluoromethyl, nitro, or amino, when p is 1;

Y is lower alkoxy, hydroxy, or halogen when p is 2 and X is -O-;

 (R_1) is

-CH2-CH=CH-CH2-,

-CH₂-C≡C-CH₂-,

-CH₂-CH=CH-CH₂-CH₂-,

-CH₂-CH₂-CH=CH-CH₂-,

 $-CH_2-C = C-CH_2-CH_2-$, or

 $-CH_2-CH_2-C = C-CH_2-$

the -CH=CH- bond being cis or trans;

R is hydrogen, lower alkyl, lower alkoxy, hydrox; l, carboxyl, chlorine, fluorine, bromine, iodine, amino, lower mono or dialkylamino, nitro, lower alkyl thio, trifluoromethoxy, cyano, acylamino, trifluoromethyl, trifluoroacetyl, aminocarbonyl, dialkylaminocarbonyl, formyl,

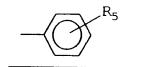
November 3, 2004 Attorney Docket No. P25,984-A REI

-C(=O)-alkyl, -C(=O)-O-alkyl, -C(=O)-aryl, -C(=O)-heteroaryl,

-CH(OR₇)-alkyl, -C(=W)-alkyl, -C(=W)-heteroaryl;

where alkyl is lower alkyl;

aryl is phenyl or



where R₅ is hydrogen, lower alkyl, lower alkoxy, hydroxy, chlorine, fluorine, bromine, iodine, lower monoalkylamino, lower dialkylamino, nitro, cyano, trifluoromethyl, trifluoromethoxy;

heteroaryl is

$$Q_3$$

where Q₃ is -O-, -S-, -NH-, or -CH=N-;

W is CH, or CHR, or N-R,

R₇ is hydrogen, lower alkyl-(C=O)-:

R₈ is lower alkyl;

Ro is hydroxy, lower alkoxy, or -NHR 10; and

R₁₀ is hydrogen, lower alkyl, C₁-C₃ acyl, aryl,

November 3, 2004 Attorney Docket No. P25,984-A REI

-C(=O)-aryl, or -C(=O)-heteroaryl,

where aryl and heteroaryl are as defined above; and

m is 1, 2, or 3;

- with the exclusion of compounds wherein X is O or S, Y is hydrogen, and R is hydrogen, $C_1-C_4 \text{ alkyl, chlorine, fluorine, bromine, iodine, cyano, } C_1-C_4 \text{ alkoxy, or -COOR}_{23}$ where R_{23} is C_1-C_4 alkyl;
- all geometric, optical and stereoisomers thereof, or a pharmaceutically acceptable acid

 addition salt thereof, in an amount sufficient to produce a pain-relieving effect,

 and a pharmaceutically acceptable carrier therefor.
- 93. (Amended) An analgesic composition, which comprises a compound of the formula

$$(Y)_p$$
 $N-(R_1)-O$
 $N-(R_1)$

wherein

X is -O-, -S-, -NH-, or -N(R_2);

R, is selected from the group consisting of lower alkyl, aryl lower alkyl, aryl, (C₃-

November 3, 2004 Attorney Docket No. P25,984-A REI

C₁₀)cycloalkyl, aroyl, (C₂-C₁₁)alkanoyl, and phenylsulfonyl groups;

aryl is defined hereinafter;

p is 1 or 2;

Y is hydrogen, lower alkyl, hydroxy, chlorine, fluorine, bromine, iodine, lower alkoxy, trifluoromethyl, nitro, or amino, when p is 1;

Y is lower alkoxy, hydroxy, or halogen when p is 2 and X is -O-;

 (R_1) is R_{20} or R_{21} in which one or more carbon atoms of R_{20} or R_{21} are substituted by at least one C_1 - C_6 linear alkyl group, phenyl group or

$$\text{lower alkyleneyl} \longrightarrow (Z_1)_p$$

where Z_1 is lower alkyl, -OH, lower alkoxy, -CF₃, -NO₂, -NH₂ or halogen; R_{20} is -(CH₂)_n-, where n is 2, 3, 4 or 5;

 R_{21} is

-CH₂-CH=CH-CH₂-,

 $-CH_2-C \equiv C-CH_2-$

-CH₂-CH=CH-CH₂

-CH₂-CH₂-CH=CH-CH₂-,

 $-CH_2-C \equiv C-CH_2-CH_2-$ or

-CH₂-CH₂-C≡C-CH₂-,

the -CH=CH- bond being cis or trans;

R is hydrogen, lower alkyl, lower alkoxy, hydroxyl, carboxyl, chlorine, fluorine, bromine, iodine, amino, lower mono or dialkylamino, nitro, lower alkyl thio, trifluoromethoxy, cyano, acylamino, trifluoromethyl, trifluoroacetyl, aminocarbonyl, monoalkylaminocarbonyl, dialkylaminocarbonyl, formyl, -C(=O)-alkyl, -C(=O)-O-alkyl, -C(=O)-aryl, -C(=O)-heteroaryl, -CH(OR₇)-alkyl, -C(=W)-alkyl, -C(=W)-aryl, or -C(=W)-heteroaryl;

where alkyl is lower alkyl;

aryl is phenyl or

$$R_5$$

where R₅ is hydrogen, lower alkyl, lower alkoxy, hydroxy, chlorine, fluorine, bromine, iodine, lower monoalkylamino, lower dialkylamino, nitro, cyano, trifluoromethyl, trifluoromethoxy;

heteroaryl is

$$Q_3$$

where Q₃ is -O-, -S-, -NH-, or -CH=N-;

W is CH2 or CHR8 or N-R9;

November 3, 2004 Attorney Docket No. P25,984-A REI

R₇ is hydrogen, lower alkyl, or acyl;

R₈ is lower alkyl;

R₉ is hydroxy, lower alkoxy, or -NHR₁₀; and

R₁₀ is hydrogen, lower alkyl, C₁-C₃ acyl, aryl,

-C(=O)-aryl, or -C(=O)-heteroaryl,

where aryl and heteroaryl are as defined above; and

m is 1, 2, or 3;

with the exclusion of compounds wherein X is O or S, Y is hydrogen, and R is hydrogen, $C_1-C_4 \text{ alkyl, chlorine, fluorine, bromine, iodine, cyano, } C_1-C_4 \text{ alkoxy, or -COOR}_{23}$ where R_{23} is C_1-C_4 alkyl;

with the exclusion of compounds wherein X is -S-, R₁ is R₂₀, R is H, and m=1;

all geometric, optical and stereoisomers thereof, or a pharmaceutically acceptable acid

addition salt thereof, in an amount sufficient to produce a pain-relieving effect,

and a pharmaceutically acceptable carrier therefor.

November 3, 2004 Attorney Docket No. P25,984-A REI

96. (Amended) A compound of the formula

wherein

X is -O-, -S-, -NH-, or -N(R_2);

 R_2 is selected from the group consisting of lower alkyl, aryl lower alkyl, aryl, $(C_3$ - C_{10})cycloalkyl, aroyl, $(C_2$ - C_{11})alkanoyl, and phenylsulfonyl groups; aryl is as defined hereinafter;

p is 1 or 2;

Y is hydrogen, lower alkyl, hydroxy, chlorine, fluorine, bromine, iodine, lower alkoxy, trifluoromethyl, nitro, or amino, when p is 1;

Y is lower alkoxy, hydroxy, or halogen when p is 2 and X is -O-;

n is 2, 3, 4 or 5;

R is hydrogen, lower alkyl, lower alkoxy, hydroxyl, carboxyl, chlorine, fluorine, bromine, iodine, amino, lower mono or dialkylamino, nitro, lower alkyl thio, trifluoromethoxy, cyano, acylamino, trifluoromethyl, trifluoroacetyl, aminocarbonyl, dialkylaminocarbonyl, formyl, -C(=O)-alkyl, -C(=O)-O-alkyl,

November 3, 2004 Attorney Docket No. P25,984-A REI

-C(=O)-aryl, -C(=O)-heteroaryl, or -CH(OR₇)-alkyl; -C(=W)-alkyl, -C(=W)-aryl, or -C(=W)-heteroaryl;

alkyl is lower alkyl;

aryl is phenyl or

$$- \bigcirc \stackrel{R_5}{\longrightarrow}$$

where R₅ is hydrogen, lower alkyl, lower alkoxy, hydroxy, chlorine, fluorine, bromine, iodine, lower monoalkylamino, lower dialkylamino, nitro, cyano, trifluoromethyl, or trifluoromethoxy;

heteroaryl is

$$- \boxed{\mathbb{Q}_3}$$

 Q_3 is -O-, -S-, -NH-, or -CH=N-;

W is CH₂ or CHR₈ or N-R₉;

R₇ is hydrogen, lower alkyl, or lower alkyl-(C=O)-:

R₈ is lower alkyl;

R₉ is hydroxy, lower alkoxy, or -NHR₁₀; and

November 3, 2004 Attorney Docket No. P25,984-A REI

 R_{10} is hydrogen, lower alkyl, C_1 - C_3 acyl, aryl, -C(=O)-aryl or -C(=O)-heteroaryl,

where aryl and heteroaryl are as defined above; and

m is 1, 2, or 3;

with the proviso that at least one R is selected from the group consisting of

dialkylaminocarbonyl, formyl, -C(=W)-alkyl, -C(=W)-aryl, and

-C(=W)-heteroaryl;

with the exclusion of compounds wherein X is O or S, Y is hydrogen, and R is hydrogen, C_1 - C_4 alkyl, chlorine, fluorine, bromine, iodine, cyano, C_1 - C_4 alkoxy, or -COOR₂₃ where R_{23} is C_1 - C_4 alkyl;

with the exclusion of compounds wherein X is -S-, R is H, and m=1;

all geometric, optical and stereoisomers thereof, or a pharmaceutically acceptable acid addition salt thereof.